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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,357	12/12/2005	Hiroshi Tomiyama	TAN-356	8894

7590 01/28/2010

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EXAMINER	
BLAND, LAYLA D	
ART UNIT	PAPER NUMBER
1623	
MAIL DATE	DELIVERY MODE
01/28/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,357	TOMIYAMA ET AL.	
	Examiner	Art Unit	
	LAYLA BLAND	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4 and 29-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 29-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is a response to Applicant's amendment submitted October 26, 2009, wherein claims 4, 30, and 32 are amended and claims 1-3, 5-28, and 33 are canceled. Applicant's declaration of Kazuhiro Kosakai submitted October 26, 2009 under 37 CFR 1.132, is acknowledged and will be further discussed below.

Claims 4 and 29-32 are pending and are examined on the merits herein.

In view of Applicant's amendment submitted October 26, 2009, the rejection of claims 30, 32, and 33 under 35 U.S.C. 112, second paragraph is withdrawn because "administered" was removed from the claims.

The following rejection is maintained:

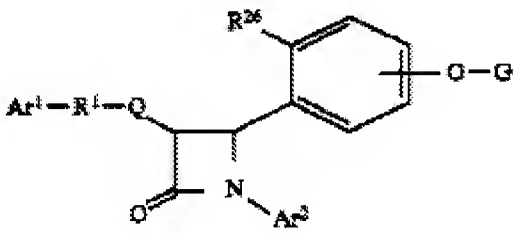
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4 and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yumibe et al. (US 5,756,470, May 26, 1998, of record) and Tomiyama et al. (US 2004/0063929, April 1, 2004, PTO-1449 submitted April 25, 2006, English equivalent of WO02/066464, published August 29, 2002, of record).

Yumibe et al. teaches a combination of a cholesterol biosynthesis inhibitor and a β-lactam cholesterol absorption inhibitor for lowering cholesterol and treating or preventing atherosclerosis [see abstract]. Suitable HMG CoA reductase inhibitors include lovastatin, pravastatin, fluvastatin, and simvastatin [column 10, lines 24-27 and claim 17]. The genus of compounds taught by Yumibe et al. is as follows [column 2]:

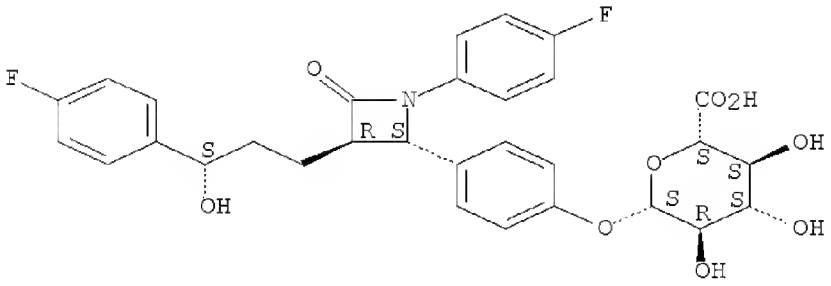


Wherein R^{26} is H or O-sugar, G is a sugar, and Ar^1 and Ar^2 are aryl or substituted aryl. Specific embodiments are claimed in claim 13 and include the following:

L2 ANSWER 26 OF 45 REGISTRY COPYRIGHT 2008 ACS on STN
RN 190448-57-8 REGISTRY
ED Entered STN: 27 Jun 1997
CN β-D-Glucopyranosiduronic acid, 4-[(2S,3R)-1-(4-fluorophenyl)-3-[(3S)-3-(4-fluorophenyl)-3-hydroxypropyl]-4-oxo-2-azetidinyl]phenyl (CA INDEX NAME)

OTHER NAMES:
CN Sch 58235 glucuronide
CN Sch 60663
FS STEREOSEARCH
MF C30 H29 F2 N O9
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, PROUSDDR, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.

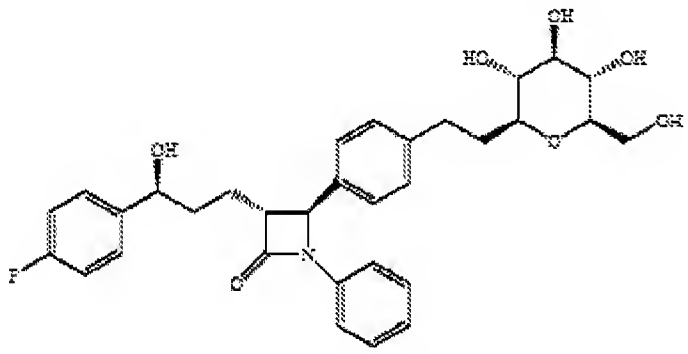


Pharmaceutical compositions comprising the compounds of Yumibe et al. and a lovastatin, pravastatin, fluvastatin, or simvastatin are specifically claimed [claims 17]. The pharmaceutical compositions can be administered in forms such as capsules, tablets, powders, etc., and can include excipients such as fillers, binders, buffers, etc. [column 17, lines 11-23]. The daily dose of the compound is about 0.001-30 mg/kg per day [column 17, lines 24-26]. The daily dose of the HMG reductase inhibitor administered in combination with the compound is 0.1-80 mg/kg per day in single or divided doses [column 17, lines 33-41]. The components may be administered separately [column 17, lines 49-51].

The difference in the beta-lactams taught by Yumibe et al. and the instantly claimed beta-lactams is that the instantly claimed lactams comprise C-glycosides and those of Yumibe et al. comprise O-glycosides.

Tomiyama et al. teach beta-lactam compounds which are useful as serum cholesterol-lowering agents [see abstract]. One preferred compound, compound 56 [page 18], shown below, is the same compound as that which is recited in instant claim 4:

56



Hypocholesterolemic beta-lactam-O-glucuronic acid conjugate derivatives are known, but the O-glycoside bonds in beta-lactam-O-glucuronate compounds can be hydrolyzed in the small intestine, possibly reducing the activity of the compounds [0003-0004]. Thus, hybrid beta-lactams having a C-glycoside, which is stable to metabolism by glycosidase and hydrolysis, were prepared [column 2, lines 3-10]. The compounds are excellent hypocholesterolemic agents and are expected to have reduced side effects compared to the O-glycoside compounds [0006].

Tomiyama et al. do not teach a combination of beta-lactam and HMG-CoA reductase inhibitor.

It would have been obvious to one of ordinary skill in the art to prepare a cholesterol-lowering composition comprised of a HMG-reductase inhibitor and a β-lactam taught by Tomiyama et al. The combination of beta-lactam cholesterol absorption inhibitor and HMG-reductase inhibitor is already known in the art, as taught by Yumibe et al. Tomiyama et al. teach modified beta-lactams comprising C-glycosides which are improved over Yumibe's O-glycosides, as discussed above. One of ordinary skill in the art could have substituted Tomiyama's modified beta-lactams for the beta-lactams in the combination taught by Yumibe et al. and would have predicted that the resulting composition would be effective for reducing plasma cholesterol levels and treating atherosclerosis.

Further, both cholesterol biosynthesis inhibitors and the β-lactams taught by Tomiyama et al. are known in the art for reducing serum cholesterol levels. It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose. In re Kerkhoven, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

Response to Arguments

Applicant argues that the combination of the compound of claim 4 and HMG-CoA reductase inhibitor displays a greater synergistic effect than would be expected in view of the prior art, and that the combination is effective for lowering serum cholesterol levels. The declaration of Kazuhiro Kosakai submitted October 26, 2009 shows that the claimed compound in combination with either atorvastatin or rosuvastatin shows a

greater synergistic effect than the combination of the prior art compound 56 with the same statins. However, this data is not commensurate in scope with the claims, which are drawn to any HMG-CoA reductase inhibitor or one of many recited in claim 29. See MPEP 716.02(d): Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In other words, the showing the unexpected results must be reviewed to see if the results occur over the entire claimed range. In this case, statins are known to have different pharmacological effects and drug interactions. Please see the Bellosta reference, attached herein for Applicant's convenience. Thus, the results presented in the Kazuhiro Kosakai could not be reasonably expected to occur over the entire claimed range of HMG-CoA reductase inhibitors. For this reason, the rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Layla Bland/
Examiner, Art Unit 1623

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623